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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/893,321	06/27/2001	D. Wade Walke	LEX-0195-USA	2099

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EXAMINER
LANDSMAN, ROBERT S

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 03/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/893,321	Applicant(s) WALKE ET AL.	
	Examin r Robert Landsman	Art Unit 1647	

-- The MAILING DATE of this c mmunication appears on the c ver sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5,6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence Comparisons A and B* .

DETAILED ACTION

1. Formal Matters

A. Claims 1-4 are pending and were subject to restriction in Paper No. 7, mailed 9/3/02. In Paper No. 8, filed 10/8/02, Applicants elected Group I with traverse and argued that since SEQ ID NO:3 is entirely contained within SEQ ID NO:1, the search would not be undue. In view of this argument, all claims, which include SEQ ID NO:1-4, will be searched.

B. The Information Disclosure Statement, filed 11/29/01, has been entered into the record.

C. The Information Disclosure Statement, filed 8/16/02, has been entered into the record.

D. Though not the basis for an objection or a rejection, the syntax of claim 1 could be improved by replacing the word "drawn" with "selected."

2. Title

A. The title is objected to since it recites the word "novel." All patents contain novel subject matter. Therefore, this term should be removed. In addition, the title recites "Human GABA receptors and polynucleotides encoding the same." However, this application is only claiming polynucleotides encoding these proteins. Therefore, the title should be amended to recite, for example, "Polynucleotides encoding GABA proteins."

3. Claim Objections

A. Claim 2 is objected to since the syntax could be improved by replacing the phrase "shown in" with "of."

B. Claims 3 and 4 are objected to since the syntax could be improved by replacing the phrase "first disclosed in" with "of."

4. Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

A. Claims 1-4 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by a specific and substantial asserted utility, or a well established utility. These claims are directed to an

isolated nucleic acid comprising at least 24 contiguous bases of SEQ ID NO:1, or 3, nucleic acid molecules which encode the protein of SEQ ID NO:2, or 4 and those which hybridize to SEQ ID NO:1, or to the complement thereof. However, the invention encompassed by these claims has no apparent or disclosed patentable utility. This rejection is consistent with the current utility guidelines (published 1/5/01, 66 FR 1092). The instant application has provided nucleotide (SEQ ID NO:1 and 3) and protein (SEQ ID NO:2 and 4) sequences. SEQ ID NO:3 and 4 are truncated versions of SEQ ID NO:1 and 2, respectively, so only SEQ ID NO:1 and 3 will be discussed here for simplicity. The instant application does not disclose a specific and substantial biological role of the nucleic acid molecule of SEQ ID NO:1, or the protein of SEQ ID NO:2, or their significance. Therefore, no specific and substantial utility of these nucleic acid molecules, or protein can be asserted.

It is clear from the instant specification that the claimed receptor is what is termed an "orphan receptor" in the art. Applicants disclose in the specification that the receptor encoded for by the claimed nucleic acid molecule is believed to encode a protein (termed "NHP" for "novel human protein") related to animal GABA proteins (page 1, lines 9-12). However, the basis that the receptor is disclosed in the specification to be homologous to GABA proteins is not predictive of use. There is little doubt that, after complete characterization, this protein will probably be found to have a patentable utility. This further characterization, however, is part of the act of invention and, until it has been undertaken, Applicants' claimed invention is incomplete.

The instant situation is directly analogous to that of which was addressed in Brenner v. Manson, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anticancer activity was alleged to be potentially useful as an antitumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. 101, which required that an invention must have either an immediate obvious or fully disclosed "real-world" utility. The court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility," "[u]nless and until a process is refined and developed to this point - where specific benefit exists in currently available form – there is insufficient justification for permitting an applicant to engross what may prove to be a broad field," and "a patent is not a hunting license," "[i]t is not a reward for the search, but compensation for its successful conclusion."

The specification discloses that the polynucleotide of the invention (SEQ ID NO:1) encodes a protein which shares "sequence homology with animal GABA proteins." However, this is not a specific and substantial asserted utility, or a well established utility of the protein of the instant specification. No comparisons between the sequence of the protein of the present invention and any GABA protein has been disclosed in the specification, nor does the specification disclose that the protein encoded for by the polynucleotide of the present invention has biological activities similar to GABA proteins. Sequence homology alone cannot be accepted in the absence of supporting evidence, because the relevant literature acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases.

For example, Skolnick et al. (Trends in Biotech. 18:34-39, 2000) state that knowing the protein structure by itself is insufficient to annotate a number of functional classes, and is also insufficient for annotating the specific details of protein function (see Box 2, p. 36). Similarly, Bork (Genome Research 10:398-400, 2000) states that the error rate of functional annotations in the sequence database is considerable, making it even more difficult to infer correct function from a structural comparison of a new sequence with a sequence database (see especially p. 399). Such concerns are also echoed by Doerks et al. (Trends in Genetics 14:248-250, 1998) who state that (1) functional information is only partially annotated in the database, ignoring multi functionality, resulting in underpredictions of functionality of a new protein and (2) overpredictions of functionality occur because structural similarity often does not necessarily coincide with functional similarity. Smith et al. (Nature Biotechnology 15:1222-1223, 1997) remark that there are numerous cases in which proteins having very different functions share structural similarity due to evolution from a common ancestral gene. By example, PTH and PTHrP are two structurally closely related proteins which can have opposite effects on bone resorption (Pilbeam et al. Bone 14:717-720, 1993; see p. 717, second paragraph of Introduction).

Brenner (Trends in Genetics 15:132-133, 1999) argues that accurate inference of function from homology must be a difficult problem since, assuming there are only about 1000 major gene superfamilies in nature, most homologs must have different molecular and cellular functions. Finally, Bork et al. (Trends in Genetics 12:425-427, 1996) add that the software robots that assign functions to new proteins often assign a function to a whole new protein based on structural similarity of a small domain of the new protein to a small domain of a known protein. Such questionable interpretations are written into the sequence database and are then considered facts.

Therefore, based on the discussions above concerning the specific examples of structurally similar proteins that have different functions, along with the art's recognition that one cannot rely upon

structural similarity alone to determine functionality, the specification fails to teach the skilled artisan the utility of the claimed polynucleotide of SEQ ID NO:1, which is only known to encode a protein which shares "sequence homology with animal GABA proteins."

Therefore, the instant claims are drawn to a nucleic acid molecule which has a yet undetermined function or biological significance. There is no actual and specific significance which can be attributed to said nucleic acid molecule, or encoded protein, identified in the specification. For this reason, the instant invention is incomplete. In the absence of a knowledge of the natural ligands or biological significance of this protein, or any significance of the nucleic acid molecule of the present invention, which has not been disclosed in the specification as having any specific or substantial utility, there is no immediately obvious patentable use for them. To employ the nucleic acid molecule of the instant invention to treat, to better understand disease, or to use it to produce a receptor protein to identify substances which bind to and/or mediate activity of the said receptor is clearly to use it as the object of further research which has been determined by the courts to be a non-patentable utility. Since the instant specification does not disclose a "real-world" use for the nucleic acid molecule of the invention, then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. 101 as being useful.

Therefore, since the polynucleotides of SEQ ID NO:1 and 3 do not have a specific, substantial, or credible utility, or a well-established utility, then the polynucleotides comprising at least 24 contiguous bases of SEQ ID NO:1 or 3 also do not possess utility.

5. Claim Rejections - 35 USC § 112, first paragraph - enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

A. Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, as failing to adequately teach how to use the instant invention. Specifically, since the claimed invention is not supported by a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

B. Furthermore, even if the nucleic acid molecule of the present invention was shown to possess utility under 35 USC 101, claims 3 and 4 would be rejected under 35 U.S.C. 112, first paragraph, because the specification, while then being enabling for SEQ ID NO:1-4, does not reasonably provide enablement for all nucleic acid molecules comprising at least 24 contiguous bases of SEQ ID NO:1 or 3. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

First, the breadth of the claims is excessive with regard to claiming all nucleic acid molecules which comprise **"at least 24 contiguous bases"** of SEQ ID NO:1 or 3. Nucleic acid molecules comprising at least 24 contiguous bases of SEQ ID NO:1 or 3 would have one or more nucleic acid substitutions, deletions, insertions and/or additions to said nucleic acid molecules. Similarly, nucleic acid molecules which comprise at least 24 contiguous bases of SEQ ID NO:1 or 3 may encode for a protein with one or more amino acid substitutions, deletions, insertions and/or additions to the protein encoded for by SEQ ID NO:1 or 3.

Applicants provide no guidance or working examples of the nucleic acid molecule of SEQ ID NO:1 or 3, or of the protein which it encodes, nor do they provide any guidance or working examples of nucleic acid molecules which comprise at least 24 contiguous bases of SEQ ID NO:1 or 3. In addition, Applicants do not provide any *function* of these nucleic acid molecules, or of the proteins which they may encode. Furthermore, it is not predictable to one of ordinary skill in the art what the functions of these nucleic acids, or the proteins which they encode, would be.

In summary, even if Applicants were able to demonstrate that the nucleic acid molecule of SEQ ID NO:1 or 3 of the present invention possesses utility, the breadth of the claims would still be excessive with regard to Applicants claiming all nucleic acids which comprise at least 24 contiguous bases of SEQ ID NO:1 or 3. There is also a lack of guidance and working examples of these nucleic acid molecules. These factors, along with the lack of predictability to one of ordinary skill in the art as to what the function of these nucleic acid molecules are, or of the proteins which they may encode, leads the Examiner to hold that undue experimentation would still be necessary to practice the invention as claimed.

6. Claim Rejections - 35 USC § 112, first paragraph – written description

A. Claims 1 and 3 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These are genus claims. Nucleic acid molecules which comprise "at least 24 contiguous bases" of SEQ ID NO:1 or 3 would have one or more nucleic acid substitutions, deletions, insertions and/or additions to said nucleic acid molecules. The specification and claims do not indicate what distinguishing attributes are shared by the members of the genus. Thus the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. However, neither the specification, nor the claims, provides any description as to what changes should be made, aside from the limitation that the nucleic acid molecules of the genus comprise at least 24 contiguous bases of SEQ ID NO: or 3. Structural features that could distinguish compounds in the genus from others in the nucleic acid or protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, SEQ ID NO:1 or 3 alone are insufficient to describe the genus.

One of skill in the art would reasonable conclude that the disclosure fails to provide a representative number of species to describe the genus. The specification provides a written description only of SEQ ID NO:1 or 3. No other species are described, or structurally contemplated, within the instant specification. Therefore, one skilled in the art cannot reasonably visualize or predict the critical nucleic acid residues which would structurally characterize the genus of all isolated nucleic acid molecules which comprise at least 24 contiguous bases of SEQ ID NO:1 or 3, because it is unknown and not described what structurally constitutes any different nucleic acids in this genus besides the single requirement that they must comprise at least 24 contiguous bases of SEQ ID NO1 or 3; thereby not meeting the written description requirement under 35 USC 112, first paragraph. Thus, Applicant was not in possession of the claimed genus at the time the invention was made.

7. Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 2 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 2 is vague and indefinite since it recites "stringent conditions." It is not known what these conditions are. Nucleic acid molecules which hybridize under conditions of "low" stringency would not necessarily hybridize under conditions of "high" stringency. Furthermore, not all conditions of "high" or "low" stringency, for example, are the same. Therefore, it is required that Applicants amend the claims to recite the exact hybridization conditions (e.g. page 8, lines 27-30 of the specification) without using indefinite phrases such as "*for example*" and **without adding new matter**.

B. Claim 2 is also confusing since it is not clear in part (b) of the claim if the nucleic acid molecule hybridizes to the complement of SEQ ID NO:1, or if the complement is of the nucleic acid which hybridizes to SEQ ID NO:1.

8. Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

A. Claims 3 and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Ymer et al. (Accession No. X57514; reference CL on the Form PTO-1449 filed 8/16/02). The claim recites an isolated nucleic acid molecule comprising at least 24 contiguous bases of SEQ ID NO:1 or 3. Hillier et al. teach an isolated nucleic acid molecule which comprises 53 contiguous bases of SEQ ID NO:1 and 3 (see the Sequence Comparisons A and B accompanying this Office Action).

9. Conclusion

A. No claim is allowed.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (703) 306-3407. The examiner can normally be reached on Monday - Friday from 8:00 AM to 5:00 PM (Eastern time) and alternate Fridays from 8:00 AM to 5:00 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Fax draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert Landsman, Ph.D.
Patent Examiner
Group 1600
March 05, 2003